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APPLICATION FOR PATENT

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Title: MULTIPLE CRYOPROBE APPARATUS AND METHOD

This application is a continuation of U.S. Patent Application No. 09/860,486, filed May 21, 2001, which claims the benefit of priority from U.S. Provisional Patent Application No. 60/242,455, filed October 24, 2000, the disclosure thereof is incorporated herein by reference.

FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to an apparatus and method of cryoablation, and more particularly for cryoablation using multiple probes introduced into the body of a patient through a common introducer, so as to perform cryoablation of a particular volume of tissue while minimizing damage to adjacent healthy tissues.

A variety of medical conditions are preferentially treated by ablation of tissues within the body. Classically, ablation was performed using invasive surgical procedures requiring cutting or destroying tissues between the exterior of the body and the particular site whose ablation is desired. More recently, less invasive procedures have been developed, which bring about the destruction of selected tissues using a probe or probes which penetrate to the area to be operated, and destroy the selected tissue by transferring energy to those tissues; RF energy, light (laser) energy, microwave energy, and high-frequency ultra-sound energy are among the forms which have been used. However all such methods have the common disadvantage that while transferring energy to the tissues whose destruction is intended, they tend also to transfer energy, through conduction, convection, and other natural processes, to nearby healthy tissues as well. All such energy transfer methods ultimately result in heat

release, causing complications and adverse effects. Noticeable pain results, the functioning of nearby healthy tissues is impaired, and the healthy tissues are often damaged or destroyed. Moreover, in some cases tissues exposed to thermal energy or other forms of energy that raise their temperatures secrete  
5 substances that may be toxic to adjacent healthy tissues.

In contrast, cryoablation provides a number of important advantages over other ablation techniques. Cryoablation provides better control of the ablated volume than is attainable using other procedures. Moreover, real-time imaging during cryoablation, using ultrasound and MRI techniques, is helpful and  
10 straightforward, since the frozen tissue is clearly seen under these imaging techniques. Also, cryoablation, unlike heat radiation techniques, allows for repeatable and/or complementary treatment of the affected area. Cryoablation is considered to cause less pain to the patients. Some scientific evidence supports the conclusion that there is less morbidity and less risk of mortality as a result of  
15 cryoablation procedure compared to other minimally invasive and traditional techniques. For these and other reasons, cryoablation has recently become a popular method for certain types of minimally invasive ablation procedures. Examples include the treatment of prostate malignant tumors and of benign prostate hyperplasia (BPH), and the creation of trans-myocardial channels to  
20 effect trans-myocardial revascularization.

Yet, cryoablation procedures also have an inherent disadvantage. Cryoprobes when activated typically form at their tip what is known in the art as an "ice ball", a volume which is frozen by exposure to the low temperatures developed by the cryoprobe. Unfortunately, the radius of the volume in which  
25 total destruction of tissues is achieved (such destruction of tissues being the purpose of the operation) is typically only half of the radius of the volume within which tissues are more or less severely damaged. Since the volume of a sphere is proportional to the cube of the radius, the volume of total cell destruction, for a particular ice-ball, will typically be only the order of  
30 one-eighth of the volume of the area that is frozen during the operation and

more or less severely damaged. The disadvantage is clear: if a single ice-ball is used to destroy a selected volume, and the ice-ball is large enough to ensure the complete destruction of that volume (which complete destruction would be desired in the case of a malignancy, for example), then a surrounding volume  
5 approximately seven times larger will be more or less severely damaged. That surrounding volume will typically include much healthy tissue that would preferably be left healthy and intact. In the case of ablation of the prostate, for example, freezing of surrounding tissues using simple cryosurgical techniques will typically damage or destroy, and create temporary or permanent impairment  
10 of the function of, the prostatic urethra, the anus, and various bundles of nerves in the prostatic area.

One method of solving this problem is taught by U.S. Pat. No. 6,142,991 to Schatzberger, teaching the use of a series of ice-balls of small dimensions, such as can be created by a two-dimensional array of cryoprobes whose depth of  
15 penetration can be measured and controlled, so as to achieve accurate three-dimensional placement of a plurality of ice-balls, in a manner that conforms to the dimensions and form and placement of the lesion to be destroyed. In other words, Schatzberger's apparatus defines a volume of controllable form and dimension, for cryoablation. The ice-balls created by the  
20 apparatus are each of small dimensions, and they are placed so as to be contiguous to one another or to overlap each other. This arrangement results in a reduction of the amount of tissue that is damaged but not destroyed, and permits more accurate definition of the exact form and dimensions of the ablated tissue.

25 The mechanism described by Schatzberger is not, however, well adapted to every application of cryoablation. It is relatively complex, and requires penetration of the affected area by a multiplicity of individually introduced and individually handled cryoprobes. It could not be used, for example, in the context of cryoablating benign prostate hyperplasia (BPH) through the urethra, a  
30 relatively non-invasive treatment method described in U.S. Pat. Application No.

09/301,576, filed April 29, 1999, and incorporated herein by reference. That procedure requires an apparatus which is both more simple and more compact than that described by Schatzberger, in that the procedure requires the operating portion of the cryogenic apparatus to be introduced to the area of the lesion by means of a cystoscope, in order to reduce reducing trauma to healthy tissue.

Thus there is a widely recognized need for, and it would be highly advantageous to have, a method and apparatus for cryoablation that provides for the destruction of a defined volume of tissue, yet which minimizes damage to adjacent tissues. It would be further advantageous to have a method of cryoablation using an apparatus that creates such an extended volume of cryoablation yet is contained within a single introducer. It would be yet further advantageous to have such an introducer which could be introduced through an operating channel of a catheter or cystoscope, enabling it to reach the proximity of the region to be treated with a minimum of trauma to intervening tissues.

Referring now to another aspect of prior art, two-stage heating and cooling has successfully been used in surgical cryoablation systems, particularly in two-stage cooling of a high-pressure gas used to achieve cryogenic temperatures using Joule-Thomson heat exchangers. Two-stage cooling presents the advantages of more rapid and more efficient cooling than would be possible in a single Joule-Thomson cooling stage. In U.S. Pat. No. 5,993,444 to Ammar a cryogenic probe utilizes two stages of Joule-Thomson cooling to achieve low temperatures at the operating end of the probe. Ammar describes, however, a single probe so cooled.

Schatzberger, in the patent previously cited, describes two-stage cooling in a multi-probe system. In Figure 6a Schatzberger teaches a plurality of cryosurgical probes connected by flexible connectors to a common housing which includes a pre-cooling element for pre-cooling the high-pressure gas flowing to the probes, this element being preferably a Joule-Thomson heat exchanger used as a cooler. Schatzberger's system thus utilizes two-stage cooling, with pre-cooling taking place extracorporeally in the housing and a

second cooling stage taking place in each individual cryoprobe. Furthermore, the mechanism Schatzberger describes has the disadvantage that the pre-cooled gases must be transported a considerable distance between the housing and the probe, and the conduit connecting the probe to the housing, which must remain flexible, must also be thermally insulated.

Consequently, it would be further advantageous to have a cryoablation apparatus and method which enables the pre-cooling of a plurality of cryoprobes within a single introducer, such that the pre-cooling stage of a two-stage Joule-Thomson heat exchange process can take place in close proximity to a second stage of cooling which takes place within the individual cryoprobes.

#### SUMMARY OF THE INVENTION

According to one aspect of the present invention there is provided a cryosurgery apparatus comprising an introducer having a hollow and a distal portion, the distal portion being sufficiently sharp so as to penetrate into a body, the hollow of the introducer being designed and constructed for containing a plurality of cryoprobes each of the cryoprobes being for effecting cryoablation, such that each of the plurality of cryoprobes is deployable through the distal portion of the introducer when the distal portion is positioned with respect to a tissue to be cryoablated.

According to further features in preferred embodiments of the invention described below, the introducer comprises a cooling device designed and constructed to cool the hollow of the introducer, and a heating device designed and constructed to heat the hollow. The cooling device and heating device may be a combined heating/cooling device, such as a Joule-Thomson heat exchanger.

According to still further features in the described preferred embodiments, the introducer includes a heating and cooling device for pre-heating and pre-cooling gasses which are passed through at least a portion of the introducer and are subsequently delivered to at least one of the cryoprobes. The heating and cooling device will preferably be a Joule-Thomson

heat exchanger. The introducer will further comprise a heat-exchanging configuration for exchanging heat between a gas passed to at least one of a plurality of cryoprobes and the heating and cooling device. A thermal sensor, such as a thermocouple, will preferably be used to monitor temperature in the  
5 hollow.

According to still further features in the described preferred embodiments, the introducer is designed and constructed to be coupled to at least one high-pressure gas source, the gas source being coupleable to a Joule-Thomson heat exchanger having a Joule-Thomson orifice in the  
10 introducer. The gas source may be a source of at least one gas selected from a group consisting of high-pressure argon, high-pressure nitrogen, high-pressure air, high-pressure krypton, high-pressure  $\text{CF}_4$ , high-pressure  $\text{N}_2\text{O}$ , and high-pressure carbon dioxide. The gas source may also be a source of high-pressure helium. The introducer is designed and constructed so as to  
15 facilitate exchange of heat between two temperature states of gas from the high-pressure gas source, gas in a first state being at a first temperature prior to passing through the Joule-Thomson orifice, and gas in a second state being at a second temperature subsequent to passing through the Joule-Thomson orifice.

According to still further features in the described preferred  
20 embodiments, the introducer is designed and constructed to be coupled both to a first gas source and to a second gas source. The gas provided by the first gas source is cooled by expansion and may liquefy when passing through a Joule-Thomson orifice. The gas provided by the second gas source has an inversion temperature lower than the temperature obtained by liquefaction of  
25 gas provided by the first gas source. The apparatus further comprises control elements for regulating a flow of gas from the first gas source and the second gas source.

According to still further features in the described preferred embodiments, the introducer further comprises a plurality of cryoprobes  
30 contained therein. The distal end of the introducer is formed with a plurality of

openings for deployment therethrough of the cryoprobes. Preferably, at least one of the plurality of cryoprobes is coolable, and the coolable cryoprobe is also heatable. Preferably, the cryoprobes comprise a Joule-Thomson heat exchanger having a Joule-Thomson orifice, for heating and cooling the cryoprobes.

5       According to still further features in the described preferred embodiments, the hollow of the introducer is partitioned into a plurality of longitudinal compartments, each of the plurality of longitudinal compartments is designed and constructed for containing at least one of the plurality of cryoprobes.

10       According to still further features in the described preferred embodiments, the introducer comprises thermal insulation designed and constructed so as to hinder the passage of heat between the hollow of the introducer and tissues of the body, when the introducer is positioned within the body.

15       According to still further features in the described preferred embodiments, the introducer comprises a heat-exchanging configuration. The heat-exchanging configuration may include a porous matrix, which may include a conduit tunneling through at least a portion of the porous matrix, and which may include a spiral conduit integrated with the porous matrix.

20       According to still further features in the described preferred embodiments, the cryoprobes preferably comprise a distal operating head which includes a thermally conductive outer sheath having a closed distal end and a chamber formed within the sheath, the operating head being adapted to be inserted into a body and to effect cryoablation thereat. The chamber serves as a  
25       reservoir for housing a fluid in contact with at least a portion of the outer sheath of the distal operating head.

      According to still further features in the described preferred embodiments, the cryoprobes are designed and constructed coupleable to at least one high-pressure gas source, and preferably to a first gas source and also to a  
30       second gas source. The first gas source provides a first gas, which is cooled by

expansion and may liquefy when passed through the Joule-Thomson orifice. A second gas from said second gas source has an inversion temperature lower than a temperature obtained by liquefaction of said first gas.

According to still further features in the described preferred  
5 embodiments, the cryoprobes are designed and constructed so that gas from the high-pressure gas source, while in a first temperature state prior to passing through a Joule-Thomson orifice, exchanges heat with gas from the high-pressure gas source which is in a second temperature state subsequent to having passed through the Joule-Thomson orifice. Control elements are  
10 provided for regulating the flow of gas from the first gas source and from the second gas source.

According to still further features in the described preferred embodiments, at least one of the plurality of cryoprobes is designed and constructed so as to expand laterally away from the introducer when deployed.  
15 Preferably, at least some of the plurality of cryoprobes are designed and constructed to advance, during deployment, in a plurality of different directions. Also preferably, each cryoprobe deploys from the introducer according to a predetermined path, and the plurality of cryoprobes are designed and constructed to be deployed laterally away from the introducer to form a  
20 predetermined arrangement of deployed cryoprobes. The plurality of cryoprobes, designed and constructed to advance from within the introducer and deploy in a lateral direction away from a periphery of the introducer, thereby define a three-dimensional cryoablation volume, which may be of predetermined shape.

25 According to still further features in the described preferred embodiments, each cryoprobe is retractable and advanceable in and out of the introducer. An advancing and retracting member may be operably coupled to one or more cryoprobe of the plurality of cryoprobes.

According to still further features in the described preferred embodiments, at least one cryoprobe of the plurality of cryoprobes has a sharp distal end.

5 According to still further features in the described preferred embodiments, at least one cryoprobe of the plurality of cryoprobes has a blunt distal end.

According to still further features in the described preferred embodiments, at least one of the plurality of cryoprobes comprises a Joule-Thomson heat exchanger. Preferably, the Joule-Thomson heat exchanger  
10 is coupled to a tube through which gasses enter the cryoprobe, the tube has an orifice located at a distal end of the tube, the orifice opens into a sheath which includes a thermally conductive material designed and constructed to conduct heat when the cryoprobe is in contact with a body tissue to be cryoablated. Preferably, the Joule-Thomson heat exchanger comprises a coiled tube housed  
15 within the thermally conductive sheath, and the Joule-Thomson heat exchanger further comprises a gas supply line on its proximal end and a gas outlet on its distal end, the outlet being in fluid communication with a chamber.

According to still further features in the described preferred embodiments, at least one of the plurality of cryoprobes comprises a  
20 heat-exchanging configuration. The heat exchanging configuration may include a porous matrix, which may include a conduit tunneling through at least a portion of the porous matrix, and which may include a spiral conduit integrated with the porous matrix.

According to still further features in the described preferred  
25 embodiments, at least one of the plurality of cryoprobes comprises a thermal sensor for monitoring local temperature conditions in areas in close proximity to the sensor. Preferably, at least one of the plurality of cryoprobes further comprises a feedback control system coupled to a gas source and to the thermal sensor, the feedback system is responsive to a detected characteristic from the  
30 thermal sensor and serves for controlling a rate of delivery of gas from the gas

source to the cryoprobe. The thermal sensor is preferably positioned at the distal end of the cryoprobe, and may include a thermocouple.

According to still further features in the described preferred embodiments, at least one of said plurality of cryoprobes comprises a shape memory alloy material. The shape memory alloy material displays stress induced martensite behavior at a deployed position. The shape memory alloy material is in a non-stress induced martensite state when said cryoprobe is positioned in the introducer prior to deployment of the cryoprobe outside the introducer. Preferably the shape memory alloy material is an alloy of nickel titanium.

According to still further features in the described preferred embodiments, a cross section of each of said plurality of cryoprobes is between 0.3 mm and 3 mm.

According to another aspect of the present invention there is provided a method of cryosurgery comprising: (a) introducing into a body of a patient an introducer having a hollow and a distal portion being sufficiently sharp so as to penetrate into the body of the patient, the hollow of the introducer containing a plurality of cryoprobes each being capable of effecting cryoablation, each of the plurality of cryoprobes is deployable through the distal portion of the introducer; (b) deploying at least one of the plurality of cryoprobes; and (c) cryoablating a tissue of the patient with at least one of the plurality of cryoprobes.

According to further features in preferred embodiments of the invention described below, the step of cryoablating a tissue of the patient with at least one of the plurality of cryoprobes is accomplished by supplying a high-pressure gas to at least one of the plurality of cryoprobes, and cooling the cryoprobe by passing the gas through a Joule-Thomson orifice in a Joule-Thomson heat exchanger within the cryoprobe.

According to still further features in the described preferred embodiments, the cryosurgery method further comprises the step of cooling the gas within the body of the introducer prior to passing the gas through a

Joule-Thomson orifice in the Joule-Thomson heat exchanger within the cryoprobe.

According to still further features in the described preferred embodiments the cryosurgery method further comprises heating at least one of the plurality of cryoprobes prior to removing the cryoprobe from a site of  
5 cryoablating of a tissue of the patient.

According to still further features in the described preferred embodiments the cryosurgery method further comprises the step of deploying at least several cryoprobes, thereby defining a three dimensional cryoablation  
10 volume, and cryoablating the volume so defined. Preferably, an imaging device is used to position at least one of the plurality of cryoprobes with respect to a tissue to be cryoablated. Preferably, the imaging device is selected from the group consisting of an ultrasound device, a computerized tomography (CT) device, a closed magnetic resonance imaging (MRI) device, an open magnetic  
15 resonance imaging (MRI) device, a fluoroscope device and an X-ray device.

According to still further features in the described preferred embodiments the cryosurgery method further comprises the step of inducing fast cyclical temperature changes in a deployed cryoprobe, such that a temperature of said probe alternates rapidly between a temperature of approximately 0 °C  
20 and a temperature below - 40 °C.

The present invention successfully addresses the shortcomings of the presently known configurations by providing a method and apparatus for cryoablation that provides for the destruction of a defined volume of tissue, yet minimizes damage to adjacent tissues.

25 The present invention further successfully addresses the shortcomings of the presently known configurations by providing a method of cryoablation using an apparatus that creates an extended volume of cryoablation yet is contained within a single introducer.

The present invention still further successfully addresses the  
30 shortcomings of the presently known configurations by providing an apparatus

having an introducer which could be introduced through an operating channel of a catheter or cystoscope, enabling it to reach the proximity of the region to be treated with a minimum of trauma to intervening tissues.

5 The present invention yet further successfully addresses the shortcomings of the presently known configurations by providing a cryoablation apparatus and method which enables the pre-cooling of a plurality of cryoprobes within a single introducer, such that the pre-cooling stage of a two-stage Joule-Thomson heat exchange process can take place in close proximity to a second stage of cooling which takes place within the individual cryoprobes.

10 Implementation of the method and the apparatus of the present invention involves performing or completing selected tasks or steps manually, automatically, or a combination thereof. Moreover, according to actual instrumentation and equipment of preferred embodiments of the method and apparatus of the present invention, several selected steps could be implemented  
15 by hardware or by software on any operating system of any firmware or a combination thereof. For example, as hardware, control of selected steps of the invention could be implemented as a chip or a circuit. As software, control of selected steps of the invention could be implemented as a plurality of software instructions being executed by a computer using any suitable operating system.  
20 In any case, selected steps of the method of the invention could be described as being controlled by a data processor, such as a computing platform for executing a plurality of instructions.

#### BRIEF DESCRIPTION OF THE DRAWINGS

25 The invention is herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of  
30 providing what is believed to be the most useful and readily understood

description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art  
5 how the several forms of the invention may be embodied in practice.

In the drawings:

FIG. 1 is an introducer for introducing a plurality of cryoprobes into a body for effecting cryoablation, according to the present invention;

FIG. 2 is a is a schematic side view, partially in longitudinal  
10 cross-section, of an exemplary cryoprobe according to the present invention;

FIG. 3 is a schematic depiction showing mechanisms for control of delivery of high-pressure gases to a plurality of Joule-Thomson heat exchangers, according to the present invention; and

FIG. 4 is a detail view of a part of an introducer for introducing a  
15 plurality of cryoprobes into a body for effecting cryoablation, showing a Joule-Thomson heat exchanger within the introducer, according to the present invention.

#### DESCRIPTION OF THE PREFERRED EMBODIMENTS

20 The present invention is of a cryosurgical apparatus and method of cryosurgery. Specifically, the present invention can be used to effect cryoablation of selected tissues of a patient. In particular, the apparatus and method of the invention provide for the cryoablation of tissues with a minimum of damage to healthy tissues adjacent to the tissues to be cryoablated.

25 To enhance clarity of the following descriptions, the following terms and phrases will first be defined:

The phrase "heat-exchanging configuration" is used herein to refer to component configurations traditionally known as "heat exchangers", namely configurations of components situated in such a manner as to facilitate the  
30 passage of heat from one component to another. Examples of "heat-exchanging

configurations” of components include a porous matrix used to facilitate heat exchange between components, a structure integrating a tunnel within a porous matrix, a structure including a coiled conduit within a porous matrix, a structure including a first conduit coiled around a second conduit, a structure including one conduit within another conduit, or any similar structure.

The phrase “Joule-Thomson heat exchanger” refers, in general, to any device used for cryogenic cooling or for heating, in which a gas is passed from a first region of the device, wherein it is held under higher pressure, to a second region of the device, wherein it is enabled to expand to lower pressure. A Joule-Thomson heat exchanger may be a simple conduit, or it may include an orifice through which gas passes from the first, higher pressure, region of the device to the second, lower pressure, region of the device. It may further include a heat-exchanging configuration, for example a heat-exchanging configuration used to cool gasses from the first region of the device, prior to their expansion into the second region of the device. As is described hereinbelow, the expansion of certain gasses (referred to herein as “cooling gases”) in a Joule-Thomson heat exchanger, when passing from a region of higher pressure to a region of lower pressure, causes these gasses to cool and may cause them to liquefy, creating a cryogenic pool of liquefied gas. This process cools the Joule-Thomson heat exchanger itself, and also cools any thermally conductive materials in contact therewith. As further described hereinbelow, the expansion of certain other gasses (referred to herein as “heating gasses”) in a Joule Thompson heat exchanger causes the gas to heat, thereby heating the Joule-Thomson heat exchanger itself and also heating any thermally conductive materials in contact therewith.

The principles and operation of a cryosurgical apparatus and method according to the present invention may be better understood with reference to the drawings and accompanying descriptions.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details

of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

Cryoablation is typically performed in cases where a tissue of a patient has been diagnosed as undergoing inappropriate, e.g., malignant or benign, growth or development. Cryoablation might be used, for example, in the case of a malignant tumor, or in the case of a non-malignant mass compressing healthy tissues, thereby disturbing the normal functioning thereof. The operation might typically be performed in tissues of the prostate, kidney, lung, liver, bone, or breast, or in other tissues. In these and similar cases, cryoablation may be used to destroy the offending tissues.

Referring now to the drawings, Figure 1 illustrates the basic principle of the invention herein described. An introducer **100** in accordance with the teachings of the present invention, is designed and constructed so as to be sufficiently sharp, so as to easily penetrate through body tissue, inflicting minimal damage to nearby tissues. Introducer **100** has a hollow **102**. Hollow **102** is designed and constructed for containing a plurality of cryoprobes **104**. Each of cryoprobes **104** is capable of being cooled to a low temperature, say - 60 to - 120 °C, or preferably less, and is capable of freezing tissues, for effecting cryoablation.

A distal portion **106** of introducer **100** is formed with a plurality of openings **110**. As is further detailed hereinbelow, openings **110** of introducer **100** serve for deployment therethrough of a plurality of cryoprobes **104**. Each of cryoprobes **104** contained within introducer **100** is deployable outside introducer **100**, and in the deployed state is capable of effecting cryoablation. Hollow **102** may optionally be partitioned into a plurality of longitudinal compartments **112**, each compartment **112** is designed and constructed for

containing at least one, preferably one, cryoprobe 104. Hollow 102 of introducer 100 optionally includes a Joule-Thomson heat exchanger 200a (described in detail hereinbelow) for pre-heating and pre-cooling at least a portion of hollow 102, thereby cooling gasses used for heating and cooling of cryoprobes 104. External sheath 103 of introducer 100 may include thermally insulating material(s), so as to prevent heat exchange between hollow 102 of introducer 100 and tissues of the body, when introducer 100 is introduced into a body.

The mode of operation of the cryosurgery apparatus and method of the present invention involves introducing introducer 100 with its plurality of cryoprobes 104 contained within hollow 102 into the body of a patient, then, deploying through openings 110 present at distal portion 106 of introducer 100 at least one of cryoprobes 104, and cooling the deployed cryoprobe or cryoprobes 104 to perform cryoablation.

The image of introducer 100 has been expanded in Figure 1, so as to enhance visibility of details, yet introducer 100 is preferably thin in construction, so as to permit its introduction into the body in a manner that minimizes damage to tissues present along its penetration path, leading to the intended site of cryoablation. Preferably a cross-section of sheath 103 will not exceed 6 mm. In a presently preferred mode of operation, cryoprobes 104 are initially positioned within the introducer (i.e., retracted) so that they do not hinder the penetration of the introducer into the body of the patient. Each cryoprobe 104 is designed and constructed deployable through openings 110 present at distal portion 106 of introducer 100, when distal portion 106 is appropriately positioned with respect to a tissue to be cryoablated. An optional deploying and retracting member 114, shown in Figure 1 operably coupled to a cryoprobe 104a, may be operably coupled to some or all of cryoprobes 104. For most applications it will be convenient for cryoprobes 104 to be provided with sharp distal end 116 to aid in penetration of tissues during deployment, yet

under some circumstances a cryoprobe **104** with a blunt or rounded distal end **118** may preferably be used.

In a preferred embodiment each of cryoprobes **104** has a cross section of between 0.3 mm and 3 mm. In their undeployed, retracted, state, cryoprobes **104** will fit in the space made available for them within hollow **102** of introducer **100**. This allows introducer **100** to penetrate the body of a patient with little hindrance. Once at the desired cryoablation site, some or all of cryoprobes **104** are deployed beyond introducer **100**, penetrating further into the body's tissues, at which time cryoablation is performed.

In one preferred embodiment of the invention, cryoprobes **104** are designed and constructed to advance, during deployment, in a plurality of different directions. Generally, some of the cryoprobes are designed and constructed so as to expand laterally away from the introducer when deployed. As cryoprobes **104** so designed and constructed advance from within introducer **100** and deploy in a lateral direction away from the periphery of introducer **100**, they thereby define a three-dimensional cryoablation volume.

In a preferred embodiment of the present invention, cryoprobes **104** are partly constructed of shape memory alloy material, such as nitinol, a nickel titanium alloy. In typical use, shape memory alloy material used in cryoprobe **104** displays stress induced martensite behavior when cryoprobe **104** is at its deployed position.. Also in typical use, shape memory alloy material used in cryoprobe **104** is in a non-stress induced martensite state when cryoprobe **104** is positioned within introducer **100**.

The use of shape memory material in the construction of cryoprobes **104** results in each cryoprobe being characterized by a particular shape and hence a particular position with respect to the position of introducer **100**, at the time of its deployment within the body. Cryoprobes **104** may be deployed substantially to one side of introducer **100**, for cryoablation of a volume substantially located alongside introducer **100**. Alternatively, introducer **100** may be introduced into

a lesion, and cryoprobes **104** may be deployed substantially around introducer **100**, for cryoablation of a volume surrounding the position of introducer **100**. Generally, deployment of cryoprobes **104** creates a shaped volume of deployed cryoprobes, which may be a predefined shaped volume within the body.  
5 Deployed cryoprobes **104** are then cooled so as to perform cryoablation, resulting in a shaped volume of cryoablation.

It is a major advantage of the method of the present invention that a surgeon performing a cryoablation can cause the shape and position of the cryoablation volume substantially to conform to the shape and position of the  
10 tissues the surgeon desires to cryoablate. The method of the present invention permits cryoablation of exactly defined, preselected volumes.

Figure 1 provides examples of a manner in which cryoprobes deploy from introducer **100**, each according to a predetermined path, under the influence of shape memory alloy. Cryoprobe **104a**, for example, deploys  
15 laterally, from a side opening **110a** formed in distal portion **106** of introducer **100**. Cryoprobe **104b**, on the other hand, deploys in a largely forward direction, from a forward opening **110b** formed in distal portion **106** of introducer **100**. Both cryoprobe **104a** and cryoprobe **104b** illustrate deployment of a cryoprobe **104** along a predetermined path characterized by being at a specific angle with  
20 respect to introducer **100**. In a slightly different example, shape memory alloy is used to cause a cryoprobe **104c** to deploy according to a predetermined path characterized by a particular radius of curvature. Cryoprobes **104a**, **104b**, and **104c** illustrate the general principle that each of a plurality of cryoprobes **104** may be prepared for deployment and may be deployed each according to a  
25 predetermined path, such that the combination of deployed cryoprobes **104** creates a predetermined arrangement of deployed cryoprobes **104**, which together define a specific shape at a specific position in the vicinity of introducer **100**. In practice, the arrangement of cryoprobes **104** within

introducer **100** may be preselected in accordance with a predefined cryoablation task.

When deployed cryoprobes **104** are cooled to cryoablation temperatures, e.g., - 60 ° to - 160 °C, preferably - 80 ° to - 120 °C, the cooled volumes  
5 provided by each of the deployed cryoprobes **104** combine to produce a shaped cooled volume within which cryoablation is effected. This method of arranging and deploying the cryoprobes thus creates a three-dimensional cryoablation volume of a predetermined size and shape.

According to a preferred method of operation, diagnostic procedures  
10 such as medical imaging and computer simulation are used in advance of the cryosurgery operation to approximately determine the position and shape of the tissues to be cryoablated and a configuration of cryoprobes **104** which, when deployed, will define a similar shape. Cryoprobes **104** are then selected, prepared, and placed within introducer **100** in such a manner that when  
15 cryoprobes **104** are deployed they will approximately form a predetermined shape which appropriately conforms to the diagnosed shape of the tissues to be cryoablated.

In a currently preferred method of operation according to the present invention, medical imaging equipment such as X-ray, fluoroscope,  
20 computerized tomography (CT), ultrasound, MRI (open MRI in particular), or other forms of imaging equipment is used during the operation to guide the introduction of introducer **100** into the body of a patient, to guide the placement of introducer **100** in the vicinity of the site intended for cryoablation, and to guide the deployment of cryoprobes **104** at that site, thereby ensuring that the  
25 actual shape and placement of deployed cryoprobes **104** appropriately corresponds to the placement and shape of the tissues to be cryoablated. Cooling of the deployed cryoprobes **104** is then used to cryoablate a volume of tissue approximately corresponding to the predetermined shape intended to be cryoablated. This method has the advantage of minimizing the destructive

effect of the cryoablation procedure on healthy tissues in the vicinity of the cryoablated tissues.

Figure 2 illustrates an individual cryoprobe **104** according to a preferred embodiment of the present invention. Cryoprobe **104** preferably includes  
5 elongated housing **3** having a distal operating head **4** for penetrating through tissues of a patient during deployment.

Distal operating head **4** is connected to elongated housing **3** by means of an elongated member **5** substantially thin in cross section for allowing deployment into the tissues of a body. Elongated housing **3**, elongated member  
10 **5**, and other elements of cryoprobe **104** may include shape memory alloy, as described above.

As shown in Figure 2, cryoprobe **104** preferably includes a first passageway **10** extending along its length for providing gas of high-pressure to a Joule-Thomson heat exchanger **200b** located at distal operating head **4**, and a  
15 second passageway **16** for evacuating gas from the operating head to atmosphere. First passageway **10** is preferably in the form of a substantially thin tubular element extending along elongated housing **3**, elongated member **5**, and a portion of operating head **4**. As shown in the figure, the portion of first passageway **10** extending along elongated housing **3** is preferably in the form of  
20 a spiral tube **14a** wrapped around second passageway **16**, thereby constituting a heat-exchanging configuration **40a** for exchanging heat between spiral tube **14a** and second passageway **16**. The portion of first passageway **10** extending along elongated member **5** and portion of operating head **4** is preferably in the form of a straight tube **14b** received within second passageway **16**. Further as shown in  
25 the figure, tube **14b** preferably penetrates into second passageway **16** substantially adjacent the connection of elongated member **5** and housing **3**.

Further, elongated housing **3** preferably includes a third passageway **20** enclosing first and second passageways **10** and **16**, which third passageway forming a heat-exchanging configuration **40b** in the form of a heat exchanging

chamber for precooling or preheating gas flowing within spiral tube **14a** before it arrives to operating head **4**. Third passageway **20** preferably merges with second passageway **16** at the upper end of elongated housing **3** to form a common passageway **22** for releasing gas to atmosphere.

5 In an alternative construction, heat exchanging configuration **40b** may be formed as a porous matrix **42** filling or partially filling passageway **20**, with spiral tube **14a** being formed as a spiral conduit integrated into porous matrix **42** and second passageway **16** being formed as a straight conduit tunnelling through porous matrix **42**.

10 As shown in the figures, the various passageways of the device are enclosed by an insulating chamber **24** extending along housing **3** and elongated member **5**.

Preferably, a device according to the present invention provides effective cooling or heating by using Joule-Thomson heat exchangers. Thus, first  
15 passageway **10** preferably includes a plurality of orifices for passage of high-pressure gas therethrough so as to cool or heat selective portions of the device, depending on the type of gas used. Gases that may be used for cooling include argon, nitrogen, air, krypton,  $\text{CF}_4$ , xenon,  $\text{N}_2\text{O}$ , or any mixture of gases, and are referred to herein as "cooling gasses". High pressure cooling gasses are  
20 cooled by expansion when passing through a Joule-Thomson orifice, thereby providing their cooling effect. Gases that may be used for heating include helium or any mixture of gases, and are referred to herein as "heating gasses." Heating gasses have an inversion temperature lower than temperature obtained by liquefaction of cooling gas.

25 According to the embodiment shown in Figure 2, a primary Joule-Thomson heat exchanger **200b** is located at distal operating head **4**, which heat exchanger including: an orifice **6** located preferably at the end of straight tube **14b**, and a chamber **7** defined by the inner walls of head **4**. When a high-pressure cooling gas such as argon passes through orifice **6** it expands,

causing it to cool and in some cases to liquify so as to form a cryogenic pool within chamber 7 of operating head 4. The cooled expanded gas, and the cryogenic pool of liquefied gas which may form, effectively cool outer sheath 8 of operating head 4. Outer sheath 8 is preferably made of a heat conducting material such as metal for effectively freezing body tissue so as to produce the desired cryoablation effect. When a high-pressure heating gas such as helium expands through orifice 6 it heats chamber 7 of operating head 4, thereby heating outer sheath 8 of the operating head. Such heating of the operating head may be used for preventing sticking of the device to the tissue being cryoablated.

According to a preferred embodiment of the present invention cryoprobe 104 preferably includes a plurality of Joule-Thomson heat exchangers 200c for effectively precooling or preheating the gas flowing within first passageway 10. According to the embodiment shown in Figure 2, secondary Joule-Thomson heat exchanger 200c is located within housing 3, includes a chamber 21 defined by the inner walls of passageway 20, and preferably includes an orifice 18 located preferably at the lower end of spiral tube 14a. The optional spiral construction of spiral tube 14a is designed and constructed as heat-exchanging configuration 40a, facilitating the exchange of heat between spiral tube 14a and second passageway 16, and as heat-exchanging configuration 40b facilitating the exchange of heat between spiral tube 14a and passageway 20.

When a high-pressure cooling gas such as argon passes through orifice 18 it expands and is thereby cooled. The expanded gas may liquefy so as to form a cryogenic pool within chamber 21. The cooled expanded gas, and a cryogenic pool of liquefied gas which may form, effectively cool passageway 20, thereby precooling the gas flowing within spiral tube 14a. When a high-pressure heating gas such as helium expands through orifice 18 it heats chamber 21 and passageway 20, thereby effectively preheating the gas flowing within spiral tube 14a.

Thus, gas flowing through spiral tube **14a** is effectively pre-cooled or pre-heated by exchanging heat with third passageway **20**. Furthermore, the gas flowing through spiral tube **14a** and strait tube **14b** exchanges heat with second passageway **16** which contains cooled (or heated) gas coming from operating head **4**.

A cryosurgery device according to the present invention enables to effectively and quickly produce the desired freezing effect and to quickly inverse from cooling to heating so as to prevent sticking of the operating head to the tissue.

A cryosurgery device according to the present invention also enables to induce fast cyclical temperature changes in a deployed cryoprobe, such that a temperature of the probe alternates rapidly between a temperature of approximately 0 °C and a temperature below -40 °C. This cryosurgical technique has been found useful in a variety of cryosurgical situations.

According to another embodiment (not shown), first passageway **10** may include a plurality of orifices located along spiral tube **14a** and strait tube **14b**. Further, a device according to the present invention may include a plurality of Joule-Thomson heat exchangers for cooling or heating selected portions of the device, wherein each Joule-Thomson heat exchanger includes a plurality of orifices.

The heating mechanisms heretofore described, and the cooling mechanism heretofore described, may be separate mechanisms both contained within cryoprobe **104**, yet in a preferred embodiment these mechanisms are a combined heating/cooling mechanism. First passageway **10** is designed and constructed so as to be coupleable to a first gas source, supplying a high-pressure cooling gas, and also to be coupleable to a second gas source supplying high-pressure heating gas. Thus coolable cryoprobe **104** may also be heatable.

Cryoprobe **104** preferably further comprises control elements for regulating the flow of gas from the first gas source and the second gas source. In a preferred embodiment, cryoprobe **104** includes a thermal sensor **30**, such as, for example, a thermocouple, for monitoring the temperature within chamber **7** of operating head **4** at the distal portion of cryoprobe **104**. An additional thermal sensor **32** may also be used to monitor temperature within chamber **21**, or alternatively be placed at some other convenient position within cryoprobe **104** for monitoring local temperature conditions there.

Figure 3 is a schematic drawing showing mechanisms for control of delivery of high-pressure gases to the plurality of Joule-Thomson heat exchangers **200** of cryoprobes **104** and/or introducer **100** employed in context of the present invention. Thus, heat exchangers **200** of Figure 3 schematically represent individual Joule-Thomson heat exchange mechanisms herein described, such as a Joule-Thomson heat exchanger **200a** of introducer **100** shown in Figure 1 and in Figure 4, and Joule-Thomson heat exchangers **200b** and **200c** of individual cryoprobes **104** shown in Figure 2.

Each Joule-Thomson heat exchanger **200** is coupled to a passageway **202** for supplying high-pressure gas thereto. A passageway **202**, for example, would be coupled to each gas input passageway **10** of individual cryoprobes **104**, as shown in Figure 2. A passageway **202** would similarly be coupled to the gas input passageway **310** of heat exchanger **200a**, shown in detail in Figure 4.

Each heat exchanger **200** also optionally includes a thermal sensor which monitors temperatures therewithin or in its vicinity. Each such thermal sensor connects to an electrical feedback connection **204** which thereby receives information about the temperatures within heat exchangers **200**. Electrical feedback connections **204** may be direct electrical connections, or other connections capable of transmitting data, such as infra-red connections. Thus, feedback connections **204** electrically connect with thermal sensors **30** and **32** of

individual cryoprobes **104** as shown in Figure 2, and with thermal sensor **316** of introducer **100** as shown in Figure 4.

In Figure 3, high-pressure heating gas source **206** supplies gas through control valve **208** and through a one-way valve **205** to common gas feed line **220**. Optional compressor **209** may be used to compress gas from source **206** to pressures higher than that supplied by source **206**. Similarly, high-pressure cooling gas source **216** supplies gas through control valve **218** and one-way valve **205** to common gas feed line **220**. Optional compressor **219** may be used to compress gas from source **216** to pressures higher than that supplied by source **216**.

Optional control unit **230** is for controlling valves **208** and **218**, thereby controlling a flow of gas from the gas sources into common gas feed line **220**. Control unit **230** is also for controlling individual valves **232**, thereby regulating the flow of gas into each Joule-Thomson heat exchanger **200**.

Control unit **230** receives control instructions from a control input unit **240**, which may include an operator's interface and optional computational and memory systems for supplying pre-programmed instructions. Control input unit **240** may connect directly to control unit **230**, or control input unit **240** may be more or less remote from control unit **230** and communicate with control unit **230** using remote communication, such as radio or infra-red communication, or some other form of data communication. Control unit **230** may further communicate with, and receive control instructions from, a plurality of control input units **240**.

Control unit **230** also receives feedback information from feedback connections **204** reporting temperatures within heat exchangers **200** (e.g., from thermal sensors **30**, **32** and **316**) or from other parts of the apparatus. Control unit **230**, under instructions from control input unit **240** relating to the desired temperatures, opens and closes valves **208**, **218**, and **232** to control the flow of heating and cooling gasses to heat exchangers **200**.

Joule-Thomson heat exchangers **200** heat and cool individual cryoprobes **104**. Optionally, Joule-Thomson heat exchanger **200a** of introducer **100** further preheats heating gasses and precools cooling gasses as they pass through Joule-Thomson heat exchanger **200a** of introducer **100** on their way towards the  
5 Joule-Thomson heat exchangers **200b** and **200c** of individual to cryoprobes **104**.

Optional Joule-Thomson heat exchanger **200a**, which appears in a simplified form in Figure 1, is presented in additional detail in Figure 4, according to a preferred embodiment of the present invention.

Figure 4 shows a portion of an introducer **100**. Passageways **10**, which  
10 serve for passing gas from high-pressure gas sources outside introducer **100** to cryoprobes **104**, are situated near or within a chamber **304** within hollow **102** of introducer **100**. Gas input passageway **310** provides high-pressure cooling or heating gasses which pass from passageway **310** through Joule-Thomson orifice **312**, and expand into chamber **304**. Cooling gasses passing from passageway  
15 **310** through Joule-Thomson orifice **312** expand and are thereby cooled and may liquefy. Cooling gasses cooled by expansion, and a cryogenic pool of liquefied gasses which may form, cool chamber **304**. Heating gasses, which have an inversion temperature lower than the temperature obtained by liquefaction of the cooling gasses, pass from passageway **310** through Joule-Thomson orifice **312**  
20 and heat chamber **304**. The gasses are subsequently exhausted to the atmosphere through passageway **314**. Optional thermal sensor **316**, which may be a thermocouple, monitors temperatures in chamber **304** and connects to electrical feedback connection **204** shown in Figure 3.

In a preferred embodiment, heat exchanger **200a** includes a  
25 heat-exchanging configuration **40c** for facilitating exchange of heat between incoming gasses entering heat exchanger **200a** through passageway **310** and exhaust gasses being exhausted to the atmosphere through passageway **314** after passing through Joule-Thomson orifice **312**. In this embodiment passageway **310** for incoming gasses and passageway **314** for exhaust gasses are constructed

of heat conducting material, such as a metal, and are constructed contiguous to each other, or wrapped one around the other. In an alternative construction of heat-exchanging configuration 40c, passageway 314 is implemented as a porous matrix 320 through which expanded gasses are exhausted to atmosphere. In this construction, passageway 310 is implemented as conduit 322 for incoming gasses formed within porous matrix 320. Conduit 322 may be formed as a straight conduit tunneling through porous matrix 320, or it may be formed as a spiral conduit integrated with porous matrix 320.

Heating gasses being exhausted through passage 314 after having passed through Joule-Thomson orifice 312 are hotter than incoming heating gasses entering through passageway 310. Consequently, exchange of heat between passageway 310 and passageway 314 has the effect of preheating incoming heating gasses, thereby enhancing efficiency of the apparatus.

Similarly, cooling gasses being exhausted through passage 314 after having passed through Joule-Thomson orifice 312 are colder than incoming cooling gasses entering through passageway 310. Consequently, exchange of heat between passageway 310 and passageway 314 has the effect of precooling incoming cooling gasses, thereby enhancing efficiency of the apparatus.

Passageways 10 are preferably made of a thermally conducting material, such as a metal. Consequently, heating or cooling chamber 304 pre-heats or pre-cools the gasses passing through passageways 10 towards cryoprobes 104. Thus, the arrangement here described constitutes a heat-exchanging configuration 40d, for facilitating exchange of heat between heating and cooling chamber 304 and gas passing through passageways 10. In an alternate construction, heat-exchange configuration 40d is formed by implementing a portion of passageways 10 as either straight or spiral conduits tunneling through a porous matrix 46 occupying a portion of chamber 304. In yet another alternative arrangement, cryoprobes 104 themselves pass through chamber 304, resulting a similar pre-heating or pre-cooling effect. Chamber 304 may also be

designed and constructed such that heating and cooling of chamber 304 has the effect of heating and cooling all or most of hollow 102 of introducer 100, and, as a result, all or most of the contents thereof.

5           It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable  
10   subcombination.

          Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended  
15   to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the appended claims. All publications, patents and patent applications mentioned in this specification are herein incorporated in their entirety by reference into the specification, to the same extent as if each individual publication, patent or patent application was specifically and  
20   individually indicated to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall not be construed as an admission that such reference is available as prior art to the present invention.